Amendments to the Claims:

Claim 1 (Original): A method for generating hydroxylated 14-membered macrolide compounds said method comprising:

(a) producing a 14-membered aglycone template; and,

(b) feeding said aglycone template to a strain capable of hydroxylating the aglycone template at the 14 and/or 15 position.

Claim 2 (Original): The method of claim 1, wherein the strain is identified by screening a library of prokaryotes and fungal strains to identify those which are capable of hydroxylating the aglycone template at the 14 and/or 15 position.

Claim 3 (Original): The method of claim 2, wherein the strain is identified by screening a library of actinomycetes.

Claim 4 (Original): The method of claim 1, wherein the strain is selected from the group consisting of *Streptomyces eurythermus*, *Streptomyces avermitilis* and *Streptomyces rochei*.

Claim 5 (Original): The method of claim 1, wherein the strain is selected from the group consisting of *Streptomyces eurythermus* DSM 40014, *Streptomyces avermitilis* ATCC 31272 and *Streptomyces rochei* ATCC 21250.

Claim 6 (Previously Presented): The method of claim 1, wherein the strain used in step (b) is genetically engineered to express a cytochrome P450 capable of hydroxylating the starter unit region of the aglycone template.

Claim 7 (Original): The method according to claim 6, wherein the recombinant strain used in step (b) is a prokaryote.

Claim 8 (Original): The method according to claim 7, wherein the recombinant strain used in step (b) is *E. coli*.

Claim 9 (Original): The method according to claim 7, wherein the recombinant strain used in

step (b) is an actinomycete.

Claim 10 (Original): The method according to claim 9, wherein the recombinant strain used in step (b) is selected from the group consisting of *Saccharopolyspora erythraea, Streptomyces coelicolor, Streptomyces avermitilis, Streptomyces griseofuscus, Streptomyces cinnamonensis, Streptomyces fradiae, Streptomyces eurythermus, Streptomyces longisporoflavus, Streptomyces hygroscopicus, Saccharopolyspora spinosa, Micromonospora griseorubida, Streptomyces lasaliensis, Streptomyces venezuelae, Streptomyces antibioticus, Streptomyces lividans, Streptomyces rimosus, Streptomyces albus, Amycolatopsis mediterranei, Nocardia sp, Streptomyces tsukubaensis* and *Actinoplanes sp. N902-109.*

Claim 11 (Previously Presented): The method of claim 1 wherein said hydroxylated 14-membered aglycone product is isolated after step (b).

Claim 12 (Previously Presented): The method of claim 1 which additionally comprises the step of

(c) feeding the resulting hydroxylated 14-membered aglycone to a second strain which is able to add one or more sugar moieties.

Claim 13 (Original): The method of claim 12 wherein said hydroxylated aglycone produced is fed directly to the strain of step (c) with no purification step.

Claim 14 (Previously Presented): The method of claim 12 wherein the second strain naturally synthesises the desired sugar moiety or moieties and is capable of adding them to the hydroxylated 14-membered aglycone template.

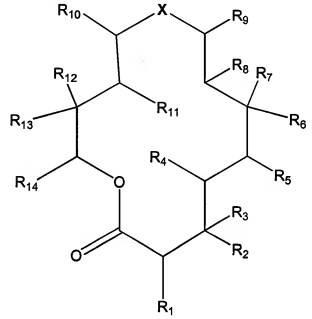
Claim 15 (Previously Presented): The method of claim 12, wherein the second strain is genetically engineered to express and / or transfer the desired sugar moiety or moieties.

Claim 16 (Original): The method of claim 15, wherein the method of genetically engineering the strain comprises introducing into said strain gene cassette(s) containing the biosynthetic genes responsible for the synthesis and / or transfer of the desired sugar moiety or moieties.

Claim 17 (Previously Presented): The method according to claim 12, wherein the strain used in step (c) is an actinomycete.

Claim 18 (Original): The method according to claim 17, wherein the strain used in step (c) is selected from the group consisting of *Saccharopolyspora erythraea*, *Streptomyces coelicolor*, *Streptomyces avermitilis*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Streptomyces fradiae*, *Streptomyces eurythermus*, *Streptomyces longisporoflavus*, *Streptomyces hygroscopicus*, *Saccharopolyspora spinosa*, *Micromonospora griseorubida*, *Streptomyces lasaliensis*, *Streptomyces venezuelae*, *Streptomyces antibioticus*, *Streptomyces lividans*, *Streptomyces rimosus*, *Streptomyces albus*, *Amycolatopsis mediterranei*, *Nocardia sp*, *Streptomyces tsukubaensis* and *Actinoplanes sp. N902-109.*

Claim 19 (Previously Presented): The method according to claim 1 wherein the aglycone template fed to said strain in step (b) is according to the formula below:

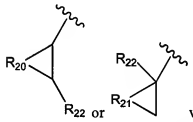


Where:

X = -C(=O)-, -CH(OH)- or $-CH_2-$, R_1, R_4, R_6, R_9, R_{10} and R_{12} are each independently H, OH, CH_3, CH_2CH_3 or OCH_3; R_2 = OH; R_3 = H; or R_2 and R_3 together are keto; R_5 = OH; R_7 = H,

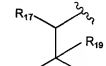
OH or OCH_3; R_8 = H, OH or keto; R_{11} = H, OH; R_{13} = H, OH, and R_{14} =  ,

 ,

 where: R_{15} is H or a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group; R_{16} is H, a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group, R_{17}, R_{18} and R_{19} are each independently H or a C_1-C_7 alkyl group or R_{20} or R_{21} are $(CH_2)_x$ where x = 2-5 and R_{22} is H; or a variant of a compound as defined above modified by replacing one or more >CHOH or >CHOMe groups by a keto group, or variant of a compound as defined above which differs in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, alkene –CH- (=CH- or -CH=), and CH_2).

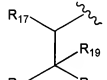
Claim 20 (Original): The method of claim 19, wherein

X = -C(=O)-, R_1 =R_4 = R_6 = R_9 = R_{10} = R_{12} = CH_3, R_2 = OH, R_7 = H, OH; R_8 = H, OH,

OCH_3; R_{11} = H, OH; R_{13} = H, OH; R_{14} =  or  , where: R_{15} = H, CH_3,or CH_2CH_3 and R_{16} is H; or R_{17} and R_{18} are each independently H or CH_3; R_{19} and R_{22} are H.

Claim 21 (Previously Presented): The method of claim 19, wherein:

X = -C(=O)-, R_1, R_4, R_6, R_9, R_{10} and R_{12} are each CH_3, R_2, R_5 and R_{11} = OH; R_3, R_8 and R_{13}=



H; R_7 = H or OH, and R_{14} = R_{18} where: R_{17}, R_{18}, R_{19} and R_{22} = H.

Claim 22 (Original): The method according to claim 6, wherein the oxidative enzyme is identified by screening a library of prokaryotic and fungal strains and cloning the range of oxidative enzymes expressed within a strain capable of hydroxylating the 14-membered aglycone template at the 14 and/or 15 position.

Claim 23 (Original): The method according to claim 22, wherein the library screened is a library of actinomycetes.

Claim 24 (Previously Presented): The method according to claim 22, wherein the range of oxidative enzymes within the strain identified as capable of hydroxylating the 14-membered aglycone template at the 14 and/or 15 position are identified using degenerate oligo primers.

Claim 25 (Previously Presented: The method according to claim 22 wherein the oxidative enzyme(s) is a cytochrome P450.

Claim 26 (Original): A method for generating hydroxylated 14-membered macrolide compounds said method comprising:

(a) producing a 14-membered aglycone template,

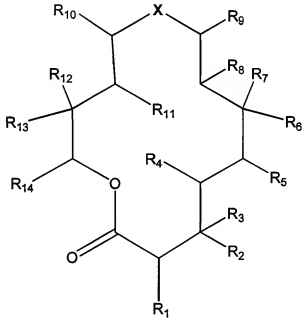
(b) identifying a cytochrome P450 capable of hydroxylating the 14-membered aglycone template at the 14 and/or 15 position by screening a library of prokaryotic and fungal strains and amplifying the range of P450s expressed within a strain,

(c) expressing and isolating said P450, and

(d) using the isolated P450 in vitro to hydroxylate the 14 and/or 15 position of said 14-membered aglycone template.

Claim 27 (Original): The method of claim 26, wherein said P450 is expressed together with appropriate ferredoxin and ferredoxin reductases.

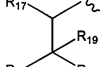
Claim 28 (Previously Presented): A process according to claim 1 which produces one or more compounds according to formula I:

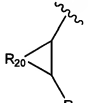


Where:

X = -C(=O)-, -CH(OH)- or $-CH_2$-, R_1, R_4, R_6, R_{10} and R_{12} are each independently H, OH, CH_3, CH_2CH_3 or OCH_3; R_2 = OH, or any glycosyl or disaccharide group, R_3 = H; or R_2 and R_3 together are keto; R_5 = OH, or any glycosyl group, R_7 = H, OH, OCH_3; R_8 = H, OH or keto; R_9, = H, OH, CH_3, CH_2CH_3 or OCH_3, *O*-megosamine, *O*-cladinose, *O*-mycarose, *O*-rhamnose or a methylated derivative thereof, *O*-digitoxose, *O*-olivose, *O*-oliose or *O*-oleandrose; *O*-desosamine, *O*-mycaminose or *O*-angolosamine; R_{11} = H, OH; R_{13} = H, OH,

and R_{14} = 

, 

, 

or 

where: R_{15} is H or a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group; R_{16} is H, a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group, R_{17}, R_{18} and R_{19} are each independently H or a C_1-C_7 alkyl group or R_{20} or R_{21} are $(CH_2)_x$ where x = 2-5 and R_{22} is O-R_{23} where R_{23} = H or a C_1 to C_7 alkyl group or C_1-C_7 acyl group; or R_{22} and R_{16} together are a keto group; or R_{22} and R_{19} together are a keto group; or a variant of a compound as defined above which differs in the oxidation state of one

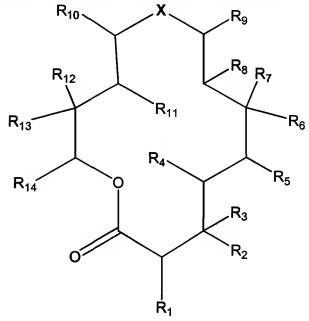
or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, alkene –CH- (=CH- or -CH=), and CH_2).

Claim 29 (Original): A process according to claim 28 wherein R_2 is selected from *O*-cladinose, *O*-mycarose, *O*-rhamnose and methylated derivatives thereof, *O*-digitoxose, *O*-olivose, *O*-oliose or *O*-oleandrose.

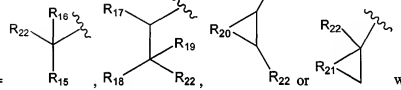
Claim 30 (Original): A process according to claim 29 wherein R_2 and/or R_9 is a said methylated derivative selected from 2'-O-methyl, 2',3'-*bis*-*O*-methyl and 2',3',4'-*tris*-*O*-methyl.

Claim 31 (Previously Presented): A process according to claim 28, wherein R_5 is a glycosyl group selected from *O*-mycaminose and *O*-angolosamine.

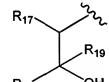
Claim 32 (Currently Amended): A compound according to formula I below:



wherein X = -C(=O)-, -CH(OH)- or $-CH_2$-, R_1, R_4, R_6, R_9, R_{10} and R_{12} are each independently H, CH_3 or CH_2CH_3, R_2 = OH or any glycosyl group; R_3 = H, or R_2 and R_3 together are keto; R_5 = OH or any glycosyl group; R_7 = H, OH, ~~OCH_3~~; R_8 = H, OH; R_{11} = H, OH, R_{13} = H, OH,

R_{14} =  where: R_{15} is H or a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group; R_{16} is H, a C_1-C_7 alkyl group or C_4-C_7 cycloalkyl group, R_{17}, R_{18} and R_{19} are each independently H or a C_1-C_7 alkyl group or R_{20} or R_{21} are $(CH_2)_x$ where x = 2-5 and R_{22} is O-R_{23} where R_{23} = H or a C_1 to C_7 alkyl group or C_1-C_7 acyl group; ~~or R_{22} = halogen or $NR_{24}R_{25}$, where R_{24} and R_{25} are each independently H, a C_1 to C_7 alkyl group or C_1-C_7 acyl group;~~ or R_{22} and R_{16} together are a keto group; or R_{22} and R_{19} together are a keto group; or a variant of a compound as defined above which differs in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, alkene –CH-, and CH_2); with the proviso that the following compounds are excluded:

(a) when R_2 = OH, *O*-cladinose or *O*-mycarose and R_5 is OH or *O*-desosamine

(b) when R_1 = R_4 = R_6 = R_9 = R_{10} = R_{12} = CH_3, R_3 = H, R_2 = *O*-oleandrose, R_5 = *O*-desosamine, R_7 = OH, R_8 = R_{13} = H and R_{14} =  , where R_{17} = R_{18} = R_{19} = H,

(c) when R_2 or R_5 = *O*-mycaminose

(d) when R_2 or R_5 = *O*-angolosamine.

Claim 33 (Original): A compound according to claim 32 wherein R_2 is selected from *O*-cladinose, *O*-mycarose, *O*-rhamnose and methylated derivatives thereof, *O*-digitoxose, *O*-olivose, *O*-oliose or *O*-oleandrose.

Claim 34 (Original): A compound according to claim 33 wherein R_2 is a said methylated derivative selected from 2'-O-methyl, 2',3'-*bis*-*O*-methyl and 2',3',4'-*tris*-*O*-methyl.

Claim 35 (Previously Presented): A compound according to claim 32, wherein R_5 is a glycosyl group selected from *O*-mycaminose and *O*-angolosamine.

Claim 36 (Previously Presented): A compound according to claim 32, where X = -C(=O)-, R_1 =R_4 = R_6 = R_9 = R_{10} = R_{12} = CH_3, R_2 = OH, *O*-rhamnose or a methylated derivative thereof, *O*-digitoxose, *O*-olivose, *O*-oliose or *O*-oleandrose, R_3 = H, R_5 = OH, *O*-mycaminose or *O*-angolosamine; R_7 = H, OH; R_8 = H, OH, OCH_3; R_{11} = H, OH; R_{13} = H, OH; R_{14} =

or


, where: R_{15} = H, CH_3,or CH_2CH_3 and R_{16} is H; or R_{17} and R_{18} are each independently H or CH_3; R_{19} is H and R_{22} is OH.

Claim 37 (Original): A compound according to claim 36, where X = -C(=O)-, R_1 =R_4 = R_6 = R_9 = R_{10} = R_{12} = CH_3, R_2 = OH, *O*-rhamnose or a methylated derivative thereof, *O*-digitoxose, *O*-olivose, *O*-oliose or *O*-oleandrose; R_3 = H; R_5 = OH, *O*-mycaminose or *O*-angolosamine; R_7 = H, OH; R_8 = H, OH, OCH_3; R_{11} = H, OH; R_{13} = H, OH; R_{14} =

or


, where: R_{15} = CH_3; R_{16} is H; or R_{17} = R_{18} = R_{19} = H and R_{22} is OH.